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BRIEF COMMUNICATION

Candidemia and Death by *Candida orthopsilosis* and *Candida metapsilosis* in Neonates and Children

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1. Introduction

Candida parapsilosis is the second most common yeast causing candidemia in children. The variable genetic composition of this taxon led to division of *C. parapsilosis* group to three different species: *C. parapsilosis*, *Candida orthopsilosis*, and *Candida metapsilosis*.[1] The incidence of infections related to *C. orthopsilosis* or *C. metapsilosis* seems to be unusual.[2]

In Brazil, there are few data on the prevalence of these two new species on candidemia episodes in pediatric patients as well as a lack of information about antifungal susceptibility profiles of *C. orthopsilosis* and *C. metapsilosis*.[3] Our study is one of the few reports made in a Brazilian pediatric hospital, but the first involving the death of neonates and children due to candidemia caused by these species.

2. Methods

A total of three cases of fungemia by *C. parapsilosis* (3 different patients) were identified in the Brazilian pediatric hospital, located in the State of São Paulo, Brazil. The patients were a 16-day old neonate, a 10-month old infant, and a 4-year old child, hospitalized for respiratory problems (infant and child) and low birth weight (neonate).

After 3 days of hospitalization the patients presented high fever chills, rapid breathing, and rapid heartbeat. They were treated with antibiotics for 5 days, but the symptoms remained. After fungemia confirmation, the patients were treated with fluconazole and amphotericin B and eventually died despite treatment.

The three isolates were analyzed phenotypically and presumptively identified as belonging to *C. parapsilosis* group, and then they were also distinguished by sequencing the internal transcribed spacer as *C. orthopsilosis* and *C. metapsilosis*.[1] This was performed according to White et al[4] and de Hoog and Gerrits van den Ende[5] Sequences were analyzed and compared with available sequences in

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GenBank using the software BLAST (http://blast.ncbi.nlm.nih.gov/Blast.cgi).

All the yeasts were studied confronting fluconazole and amphotericin B using the Etest method. The minimum inhibitory concentration (MIC) interpretation was done according to CLSI-M27A3.[6]

Ethical clearance was obtained from the Ethical Committee of the University of São Paulo. Quality control strains were included throughout the study.

3. Results

Based on the molecular analysis, two samples were identified as *C. orthopsilosis* and one as *C. metapsilosis*.

Concerning the antifungal profile of fluconazole, according to the document of CLSI-M27A3,[6] we found two susceptibility-dose dependent strains, *C. orthopsilosis* and *C. metapsilosis*. One *C. orthopsilosis* was susceptible. All the strains were susceptible to amphotericin B.

4. Discussion

The *C. parapsilosis* group is often associated with the use of the central venous catheter and parenteral nutrition, notably in childhood infections.[3] The importance of these species, as human pathogens, remains unknown. However, they have been associated with bloodstream infections or other anatomical sites. Interestingly, the incidence of *C. orthopsilosis* and *C. metapsilosis* infections has increased since 2004 with prevalence rates ranging from 2.3% to 9% and from 0.9% to 6.9%, respectively, depending on the geographical area and the clinical specimens analyzed.[1]

Cases of *C. parapsilosis* group can be found in hospitals around the world.[2,3] Although *C. parapsilosis* is the most prevalent species found in pediatric patients with candidemia, *C. metapsilosis* and *C. orthopsilosis* may also be isolated in this population, including neonates. In our study *C. orthopsilosis* was isolated from the blood of a neonate and from the blood of a child, whereas *C. metapsilosis* was isolated from only one child.

Concerning the antifungal susceptibility profile, studies *in vitro* have shown that these species are more susceptible to the most common agents used in clinic. We found that those two strains, *C. orthopsilosis* and *C. metapsilosis*, were susceptibility-dose dependent to fluconazole. Previous reports have suggested that for both species the MICs of amphotericin B and caspofungin are lower than those shown by *C. parapsilosis*. However, MICs of fluconazole are slightly higher when compared to the same species.[7]

Our study is the first in a Brazilian pediatric hospital involving death of neonates and children due to candidemia caused by these two new species. The neonates and children died even after treatment with fluconazole and amphotericin B. Therapeutic failure may be associated with the pathogenesis of infections caused by these species and this is little known. It was also noticed that the antifungal susceptibility tests revealed, *in vitro*, susceptibility of the strains; however, there was a therapeutic failure *in vivo*. Fluconazole is one of the first-line antifungal agents of choice for the treatment of candidemia in Brazilian hospitals, and this fact may be related to the increased resistance to this drug found in strains of *C. orthopsilosis* and *C. metapsilosis*.

Reports related to clinical infections with *C. orthopsilosis* and *C. metapsilosis* are not easily found in the literature, and it was not possible in this study to correlate the clinical features of infection with a particular species. Further studies are still needed to evaluate the clinical relevance of the species of this complex.

Conflicts of Interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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References

1. Tavanti A, Davidson AD, Gow NA, Maiden MC, Odds FC. *Candida orthopsilosis* and *Candida metapsilosis* spp. nov. to replace *Candida parapsilosis* groups II and III. *J Clin Microbiol* 2005;**43**:284–92.
2. Cantón E, Pemán J, Quindós G, Eraso E, Miranda-Zapico I, Álvarez M, et al. Prospective multicenter study of the epidemiology, molecular identification, and antifungal susceptibility of *Candida parapsilosis*, *Candida orthopsilosis*, and *Candida metapsilosis* isolated from patients with candidemia. *Antimicrob Agents Chemother* 2011;**55**:5590–6.
3. Ruiz LS, Khouri S, Hahn RC, da Silva EG, de Oliveira VK, Gandra RF, et al. Candidemia by species of the Candida parapsilosis complex in children's hospital: prevalence, biofilm production and antifungal susceptibility. *Mycopathologia* 2013;**175**:231–9.
4. White TJ, Bruns TD, Lee S, Taylor JW. Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. In: Innis MA, Gelfand DH, Sninsky JJ, White TJ, editors. *PCR protocols: a guide to methods and applications*. San Diego: Academic Press; 1990. p. 315–22.
5. de Hoog GS, Gerrits van den Ende AH. Molecular diagnostics of clinical strains of filamentous Basidiomycetes. *Mycoses* 1998;**41**:183–9.
6. Clinical and Laboratory Standards Institute (CLSI). *Reference method for broth dilution antifungal susceptibility testing of yeasts*. Approved standard CLSI M27-A3(28). 3rd ed. Wayne, PA: CLSI; 2008.
7. Lockhart SR, Messer SA, Pfaller MA, Diekema DJ. Geographic distribution and antifungal susceptibility of the newly described species *Candida orthopsilosis* and *Candida metapsilosis* in comparison to the closely related species *Candida parapsilosis*. *J Clin Microbiol* 2008;**46**:2659–64.